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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/937,898	Applicant(s) Goldsborough
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 1/7/02, 8/30/02,9/26/02 .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-28 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/937,898 .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 10,11
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 19- 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 19-20, the phrase "preferably" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-17, 20 and 22-28 are rejected under 35 U.S.C. 103(a) over Monforte et al. (U.S. Patent 5,700,642) (December 23, 1997) in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999).

Monforte et al teaches a method of detaching a nucleic acid molecule from a solid support to which it is attached, wherein an unconventional nucleotide is incorporated at a predetermined site in the nucleic acid molecule, the method comprising selectively cleaving the nucleic acid molecule at the site of the unconventional nucleotide (Figures 1-7 and Examples 3 and 5 and Claims 1, 17, and 18)

Monforte et al teaches a method of reversibly immobilizing a nucleic acid molecule, the method comprising:

a) incorporating an unconventional nucleotide into the nucleic acid molecule at a pre-determined site (Figures 1-5 and Examples 1-2);

b) binding the nucleic acid molecule to a solid support; steps a) and b) being carried out in either order or simultaneously; and subsequently (Figures 1-6 and Examples 1-2)

c) selectively cleaving the nucleic acid molecule at the site of the unconventional nmucleotide (Figures 1-7 and Examples 3 and 5 and Claims 1, 17, and 18).

Monforte et al teaches a method, wherein the nucleic acid molecule is a chimeric molecule comprising a nucleic acid component and another non-nucleic acid component (Figures 1-2 and Example 2).

Monforte et al teaches a method, wherein the unconventional nucleotide is uracil or ribonucleotide (Column 11, lines 5-13 and Example 4 and Figure 5D).

Monforte et al teaches a method, wherein the unconventional nucleotide is incorporated into the nucleic acid molecule as a part of a linker sequence (Figure 1 and Column 11, line 14 to Column 13, line 34).

Monforte et al teaches a method, wherein the linker sequence is a primer (Column 12, lines 16-31).

Monforte et al teaches a method, wherein the nucleic acid molecule is a primer extension product (Figure 6A).

Monforte et al teaches a method, wherein the support is a magnetic bead (Examples 2 and 5).

Monforte et al teaches a method, wherein the linker sequence is provided with means for immobilization to a solid support (Figures 1-2 and Example 2).

Monforte et al teaches a method, wherein the nucleic acid molecule is a product of an in vitro amplification reaction (Figure 6A and Claim 16, steps b) to d)).

Monforte et al teaches a method and a chimeric molecule, wherein the nucleic acid molecule comprises a linker sequence coupled to an affinity binding group or a reporter group (Examples 2 and 5 and Figure 2).

Monforte et al teaches a method of preparing a construct for binding to and subsequent cleavage from a solid support, the method comprising incorporating into the construct a nucleotide linker sequence comprising at a pre-determined site an unconventional nucleotide (Figures 1-6 and Examples 2-5).

Monforte et al teaches a poly- or oligonucleotide dU incorporating an unconventional nucleotide which is selectively cleavable (Column 20, lines 10-21 and Column 11, lines 5-13).

Monforte et al teaches a poly- or oligonucleotide, wherein the means for immobilization is biotin (Figure 5 and Column 19, lines 53-67).

Monforte et al teaches a poly- or oligonucleotide, wherein the support comprises magnetic beads (Examples 2 and 5).

Monforte et al teaches a multiplicity of oligo- or polynucleotides, wherein each different oligo- or polynucleotide incorporates a different unconventional nucleotide (Column 20, lines 10-21).

Monforte et al does not teach the selective cleaving of the nucleic acid molecule at the site of the unconventional nucleotide, wherein the selective cleavage is accomplished enzymically using a uracil DNA glycosylase enzyme.

Sutherland et al. teaches the selective cleaving of the nucleic acid molecule at the site of the unconventional nucleotide, wherein the selective cleavage is accomplished enzymically using a uracil DNA glycosylase enzyme (Column 9, lines 4-29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the selective cleaving of the nucleic acid molecule at the site of the unconventional nucleotide, wherein the selective cleavage is accomplished enzymically using a uracil DNA glycosylase enzyme of Sutherland et al. in the method of Monforte et al., since Sutherland et al. state, "The glycosylase useful in the present

invention are those that specifically cleave unconventional bases, i.e., bases other than A,G,C or T in DNA and A,G,C and U in RNA (Column 9, lines 4-6)". Sutherland et al further state, "The most preferred glycosylase in accordance with the present invention is UNG. UNG is commercially available. UNG catalyzes the excision of uracil from single or double-stranded DNA (Column 9, lines 17-21)." An ordinary practitioner would have been motivated to combine and substitute the selective cleaving of the nucleic acid molecule at the site of the unconventional nucleotide, wherein the selective cleavage is accomplished enzymically using a uracil DNA glycosylase enzyme of Sutherland et al. in the method of Monforte et al.. in order to achieve the express advantages, as noted by Sutherland et al., of glycosylase useful in the specific cleaving of unconventional bases, i.e., bases other than A,G,C or T in DNA and A,G,C and U in RNA and also in order to achieve the advantages of most preferred glycosylase UNG which is commercially available that catalyzes the excision of uracil from single or double-stranded DNA.

5. Claims 18-19 are rejected under 35 U.S.C. 103(a) over Monforte et al. (U.S. Patent 5,700,642) (December 23, 1997) in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999) further in view of Terstappen et al. (U.S. Patent 5,646,001) (July 8, 1997).

Monforte et al. in view of Sutherland et al teach the method and molecule of claims 1-17, 20 and 22-28 as described above.

Monforte et al. in view of Sutherland et al. do not teach a method for separating a target cell from a sample, the method comprising binding the target cell to a solid support by means of a chimeric molecule comprising a nucleotide linker sequence comprising a selectively cleavable

unconventional nucleotide at a pre-determined site, coupled to a functional group, wherein the functional group is an affinity binding group or antibody which binds specifically to the cell.

Terstappen et al. teach a method for separating a target cell from a sample, the method comprising binding the target cell to a solid support by means of a chimeric molecule comprising a nucleotide linker sequence comprising a selectively cleavable unconventional nucleotide at a pre-determined site, coupled to a functional group, wherein the functional group is an affinity binding group or antibody which binds specifically to the cell (Abstract, Figures 1-4, and Examples 2-7 and claims 1-5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method for separating a target cell from a sample, the method comprising binding the target cell to a solid support by means of a chimeric molecule comprising a nucleotide linker sequence comprising a selectively cleavable unconventional nucleotide at a pre-determined site, coupled to a functional group, wherein the functional group is an affinity binding group or antibody which binds specifically to the cell of Terstappen et al in the method of Monforte et al. in view of Sutherland et al., since Terstappen et al. states, "This method has medically significant diagnostic and therapeutic applications, as entire cell types can be separated from non-malignant medically vital cell types. Cancer can be diagnosed, staged, and monitored. Genetic analysis from maternal blood, CVS, or amniocentesis samples is possible. Diseases such as AIDS, tuberculosis, or hepatitis can be monitored. This invention also has utility in the fields of bone marrow transplantation, fetal cell research, in vitro

fertilization, and gene therapy (Abstract, last four sentences)". An ordinary practitioner would have been motivated to combine and substitute the method for separating a target cell from a sample, the method comprising binding the target cell to a solid support by means of a chimeric molecule comprising a nucleotide linker sequence comprising a selectively cleavable unconventional nucleotide at a pre-determined site, coupled to a functional group, wherein the functional group is an affinity binding group or antibody which binds specifically to the cell of Terstappen et al in the method of Monforte et al. in view of Sutherland et al., in order to achieve the express advantages, as noted by Terstappen et al., of a method which has medically significant diagnostic and therapeutic applications, as entire cell types can be separated from non-malignant medically vital cell types and by which cancer can be diagnosed, staged, and monitored. And by which genetic analysis from maternal blood, CVS, or amniocentesis samples is possible and diseases such as AIDS, tuberculosis, or hepatitis can be monitored and which also has utility in the fields of bone marrow transplantation, fetal cell research, in vitro fertilization, and gene therapy.

6. Claim 21 is rejected under 35 U.S.C. 103(a) over Monforte et al. (U.S. Patent 5,700,642) (December 23, 1997) in view of Sutherland et al. (U.S. Patent 5,985,619) (November 16, 1999) further in view of Stratagene Catalog (1988, Page 39).

Monforte et al. in view of Sutherland et al. expressly teach the method claims and assay reagents of claims 1-17, 20 and 22-28 as described above in detail.

Monforte et al. in view of Sutherland et al. do not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, means for introducing an unconventional nucleotide into a nucleic acid molecule and means for selective cleavage of the unconventional nucleotide wherein the means is an enzyme of Monforte et al. in view of Sutherland et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control (page 39, column 1).

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703)

306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. Any inquiry of a general nature or relating to the status of this application should be directed tithe Group analyst Chantae Dessau whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located In Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published In the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti

Patent Examiner

Art Unit 1634

February 24, 2003

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER